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Review

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Stochastic resonance model of synaesthesia

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In synaesthesia, stimulation of one sensory modality evokes additional experiences in another modality (e.g. sounds evoking colours). Along with these cross-sensory experiences, there are several cognitive and perceptual differences between synaesthetes and non-synaesthetes. For example, synaesthetes demonstrate enhanced imagery, increased cortical excitability and greater perceptual sensitivity in the concurrent modality. Previous models suggest that synaesthesia results from increased connectivity between corresponding sensory regions or disinhibited feedback from higher cortical areas. While these models explain how one sense can evoke qualitative experiences in another, they fail to predict the broader phenotype of differences observed in synaesthetes. Here, we propose a novel model of synaesthesia based on the principles of stochastic resonance. Specifically, we hypothesize that synaesthetes have greater neural noise in sensory regions, which allows pre-existing multisensory pathways to elicit supra-threshold activation (i.e. synaesthetic experiences). The strengths of this model are (a) it predicts the broader cognitive and perceptual differences in synaesthetes, (b) it provides a unified framework linking developmental and induced synaesthesias, and (c) it explains why synaesthetic associations are inconsistent at onset but stabilize over time. We review research consistent with this model and propose future studies to test its limits.

This article is part of a discussion meeting issue 'Bridging senses: novel insights from synaesthesia'.

1. Introduction

Synaesthesia is a brain-based phenomenon in which a stimulus presented to one sensory modality (the inducing sensation) triggers a simultaneous and involuntary qualitative experience in another cognitive or perceptual modality (the concurrent sensation) [1–3]. For instance, in grapheme–colour synaesthesia, present in approximately 4% of the population [4], letters and numbers evoke the experience of (or are strongly associated with) distinct colours. However, the inducer is not perceptually supplanted by the concurrent sensation, as a grapheme–colour synaesthete viewing a black number 5 would see the physical colour of the text plus additional colour qualia (e.g. a specific red hue). These experiences not only are subjectively reported by individuals but also can be characterized and verified using neuroimaging techniques. Specifically, research shows that viewing numbers or letters associated with a synaesthetic experience causes increased activation in perceptual colour areas in grapheme–colour synaesthetes, supporting the perceptual nature of the synaesthetic associations [5–7]. Notably, however, these results have not been universally replicated (see [8–10] for a critical review).

In the most fundamental sense, synaesthesia is simply one sense evoking a conscious experience in a second cognitive or perceptual modality [1,11]. As synaesthesia remains a behaviourally defined condition, researchers have argued for the expansion of this definition to include other common characteristics of synaesthesia to serve as further diagnostic criteria [2]. The most often reported aspects of these are the following: automaticity (synaesthetes have very little conscious control over the onset or content of the concurrent once

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an inducer is encountered), consistency of inducer and concurrent associations (a specific inducer is always associated with specific concurrent (e.g. 2 is always blue)), generic nature of synaesthetic experiences (associations are relatively basic as opposed to elaborate and complex images), synaesthetic experiences are laden with affect, memorable and useful [2]. However, these aspects are only strongly *associated* with the experience of synaesthesia and their requirement as diagnostic criteria remains open to debate [12–14]. The ambiguity in what constitutes a 'genuine' form of synaesthesia has contributed to the question of whether the genetic form (developmental synaesthesia) is a phenomenon distinct from acquired or drug-induced types, with each arising through unique neural mechanisms [12,15,16].

The two most established models of synaesthesia, the disinhibited feedback model and the cross-activation model (described in greater detail below), suggest competing mechanisms to explain the most important aspect of synaesthesia: that stimulation of one modality evokes activity in a second modality, leading to altered qualitative experiences. However, data in support of these models are controversial (reviewed below in detail, e.g. [6,8]), they fail to account for the broader phenotype of differences observed in synaesthetes [17–19], and they have not substantially evolved from their original proposal despite the wealth of new findings from the broader field of multisensory research. First, in §§2–5, we recount evidence for perceptual and neuroanatomical differences between synaesthetes and non-synaesthetes, as well as evidence for the broader phenotype of synaesthesia. Secondly, in §§6–9, we briefly discuss these two models, review evidence supporting them, and highlight their limitations. Finally, we propose a novel 'stochastic resonance' model of synaesthesia based on recent research that addresses the limitations of the previous models and provides a unified framework for developmental and induced synaesthesias.

Reviewed in detail in §10 of this manuscript, stochastic resonance is the process by which the addition of noise to a neural system can counterintuitively increase the quality of signal transmission or detection [20,21]. According to the stochastic resonance model of synaesthesia (SRS), the primary neurobiological difference in synaesthetes is the presence of higher levels of neural noise in the concurrent modality (usually a broad distributed network of visual areas involved in colour processing) that allows cross-modal signals to be experienced as supra-threshold conscious percepts. These increased levels of noise are also predicted to lead to the numerous altered perceptual and cognitive differences observed in the broader phenotype of synaesthesia. Furthermore, this model can explain several forms of synaesthesia—drug-induced, developmental and acquired synaesthesia—all within the same framework. We review current literature that supports this model and suggest studies to challenge its validity.

2. What makes a synaesthete different from non-synaesthete?

The defining behavioural feature of synaesthesia is that stimulation of an inducing modality (e.g. sounds) evokes qualitative experiences in an unrelated modality (e.g. colours). However, recent research has shown that there are neurobiological, perceptual and cognitive differences between synaesthetes and non-synaesthetes that are seemingly unrelated to these altered qualitative experiences [2]. In the §§3–5, we review these differences to examine whether they can be integrated with previous neurobiological models of synaesthesia.

3. Neurobiological differences (functional)

Neuroimaging studies demonstrate that synaesthetes differ from non-synaesthetes in several aspects. Most notably, inducing stimuli evoke stronger co-activation of concurrent sensory areas in synaesthetes compared with non-synaesthetes. For example, grapheme–colour synaesthetes show stronger co-activation of the visual word form area (VWFA) with perceptual colour areas (e.g. V4) [5,7]. Notably, however, these findings have not been universally replicated [8]. Furthermore, magnetoencephalography (MEG) studies show that the activation of colour regions follows activation of the VWFA by only a few milliseconds [6]. Similarly, functional connectivity is increased between grapheme and colour areas during the synaesthetic experience [22]. These co-activation findings have been expanded to other forms of synaesthesia as well. In visual–olfactory synaesthesia (images induce olfactory sensations), synaesthetic experiences were associated with primary olfactory cortex activation [23] and lexical–gustatory synaesthetes (who experience tastes on hearing specific words) showed increased activation in taste areas [24].

Neuroimaging research additionally shows that functional differences between synaesthetes and non-synaesthetes are not restricted to the inducing and concurrent modalities, nor do they require the conscious experience of synaesthesia. For example, functional connectivity between grapheme and colour areas is present even when graphemes do not induce a synaesthetic experience [22] and even during rest [25]. Furthermore, functional activation differences in grapheme–colour synaesthetes and non-synaesthetes are found not only in the corresponding sensory modalities but also in parietal and frontal regions as well (see [9,26] for review), along with increased functional connectivity between parietal and visual areas [27] and increased connectivity between the frontoparietal and visual intrinsic networks (ICNs) during resting state [25].

More generally, several studies have demonstrated that these differences are present even at hierarchically earlier levels of sensory processing. For example, grapheme–colour synaesthetes show significant differences in visual evoked potentials as measured by electroencephalography (EEG), even to stimuli that do not evoke colours. These differences occur in the primary visual areas within 70 ms, indicating differences in early processing of stimuli [19]. Similarly, studies report that synaesthesia-related activity occurs as early as V1 [28]. Thus, even basic visual cortical processes are altered in grapheme–colour synaesthesia. However, previous models of synaesthesia do not easily explain these early processing differences.

4. Neurobiological differences (anatomical)

In tandem with the functional differences, synaesthetes and non-synaesthetes demonstrate anatomical differences in these similar neural structures. Grapheme–colour synaesthetes have increased grey matter volume in the posterior fusiform gyrus (FG) [29] and increased white matter in the bilateral retrosplenial cortex [8]. Similarly, other

researchers have reported increased cortical thickness, volume and surface area in the FG and adjacent regions, such as the lingual gyrus and the calcarine cortex in grapheme–colour synaesthetes [30]. Diffusion tensor imaging (DTI) shows that grapheme–colour synaesthetes also have increased connectivity in the inferior temporal cortex, putatively in a region that could link VWFA and colour regions [31]. Similarly, sound–colour synaesthetes have greater white matter integrity in the inferior fronto-occipital fasciculus, the major white matter tract connecting visual and auditory regions [32].

However, the anatomical differences observed in synaesthetes extend beyond the inducer and concurrent modalities to numerous other neural structures. Several studies have demonstrated that synaesthetes show connectivity (as measured using DTI) and cortical thickness differences in parietal and frontal regions [31,33–36]. Synaesthetes have also been reported to possess anatomical differences in subcortical and cortical emotion processing regions of the brain [37]. More generally, synaesthetes have a globally altered structural network topology reflected by reduced small-worldness (i.e. the neural networks are more locally clustered and have a reduced long-range connectivity) [38], indicating large-scale changes exist in the brain of a synaesthete.

5. Perceptual and cognitive differences

In addition to functional and structural differences, research over the past decade indicates that synaesthetes possess a myriad of cognitive and perceptual alterations compared with non-synaesthetes. Best replicated among these are benefits on memory. For example, several studies have shown that grapheme–colour synaesthetes have an enhanced memory [39–41]. Time–space synaesthetes demonstrate similar benefits in terms of improved spatial working memory and spatial processing abilities including mental rotation [42–44]. Subjective reports suggest that these cognitive improvements are due to the recruitment of synaesthetic associations as an extra dimension to encode information, or facilitated memory processes in general [39–41,45,46].

In terms of perceptual differences between synaesthetes and non-synaesthetes, synaesthetes demonstrate enhanced perception in the concurrent modality of synaesthesia [47,48] and enhanced imagery in the concurrent [18,49–51], and have altered cortical excitability in early processing areas [17,52]. Before reviewing these perceptual differences in detail, it is important to consider how these sensory differences are causally related to the cross-sensory experiences of synaesthesia. One possibility, as argued by previous models, is that these perceptual differences are a consequence of experiencing synaesthetic associations. However, given the breadth of these perceptual changes and their presence in early sensory regions (e.g. primary visual cortex), it is also possible that these differences are not causally related to synaesthetic experiences themselves, but to the broader phenotype of synaesthesia or factors contributing to its development.

In general, the perceptual differences present in synaesthetes occur in modalities related to their synaesthetic experiences. For example, time–space synaesthetes have enhanced spatial processing abilities [42] and those with mirror-touch synaesthesia have enhanced tactile sensitivity [48]. Interestingly, grapheme–colour synaesthetes show improved colour sensitivity [47], a larger McCollough effect [53] and enhanced visual imagery [18,49,50,54]. Most importantly, these perceptual benefits are trait-like differences in synaesthetes, such that they are observed even with stimuli that do not trigger synaesthetic experiences reflecting alterations of low-level colour processing. Critically, however, studies have demonstrated reduced motion sensitivity [47] and normal non-visual imagery in synaesthetes [54], indicating that perceptual enhancements are specific to the synaesthetic concurrent modality (i.e. synaesthetes are not simply better on every task) and might have associated trade-offs. Indeed, these perceptual alterations have been associated with substantially increased cortical excitability in the primary visual cortices of synaesthetes [17,52]. Importantly, research indicates that synaesthesia can be induced in non-synaesthetes by modulating cortical excitability in primary sensory areas [55].

6. Previous models of synaesthesia

A complete neural model of synaesthesia should account for not just the localized anatomical differences observed, but also the diffuse brain-wide alterations and perceptual enhancements that are present in those with synaesthesia. Previous models of synaesthesia, the disinhibited feedback and cross-activation models, sought to explain the experience of synaesthesia in neuroanatomical terms, and provided an excellent characterization of how one sensory system could trigger activation in another. However, these models are generally unable to account for the broader phenotype of cognitive, perceptual and neuroanatomical differences that is present in synaesthesia. The following sections (§§7 and 8) review these two established models, summarizes evidence in support of them, and highlights their limitations.

7. The disinhibited feedback theory

According to the disinhibited feedback theory [11], synaesthetic experiences arise because of disinhibited feedback to the concurrent modality from higher-level brain areas where information from the inducer and the concurrent pathways converge. For example, in grapheme–colour synaesthesia, information about grapheme stimuli first propagates through the cortical hierarchy to arrive at the temporo-parietal junction. From this multisensory nexus, the signal travels back down to V4 through disinhibition of a normally inhibited feedback pathway and causes activation of a representation in V4, leading to the synaesthetic experience.

This theory makes two predictions: (a) synaesthetes and non-synaesthetes have similar brain connectivity, and (b) there is a delay between when the inducer is processed and the concurrent is activated, since it takes time for information to traverse this distributed network. The first prediction of the theory suggests that synaesthesia uses the pre-existing neural pathways in normal adults, rather than being dependent on abnormal pathways or the formation of new connections in synaesthetes. This prediction is supported by the ability of hallucinogenic drugs to induce synaesthetic experiences in non-synaesthetes [16] as well as training studies that show synaesthesia can be induced over time [56].

The second prediction suggests that in grapheme–colour synaesthesia, following presentation of a grapheme, activity will propagate from the grapheme processing areas (VWFA), to higher processing areas (possibly in parietal areas) and then backpropagate to the colour processing area

of V4. This is partially supported by the neuroanatomical differences between grapheme–colour synaesthetes and non-synaesthetes, seen in the parietal regions [27,31]. However, this model requires a substantial processing delay between activation of the VWFA and colour area V4. MEG and EEG studies, conversely, show that activity within V4 is significant within a few milliseconds after the grapheme-responsive area, and there is an absence of activation in higher processing regions before onset of activity in V4 [6]. This slight delay in the propagation of activity from grapheme to colour in synaesthesia is insufficient for signals to travel to higher processing regions and back to V4 [57,58]. However, these studies do not investigate the differences between associator and projector synaesthetes. In the light of recent connectivity research showing that the associators (and not projectors) use top-down pathways as suggested by the disinhibited feedback model [59], further research using MEG should be conducted in associator synaesthetes alone to provide more convincing evidence against the disinhibited feedback model of synaesthesia. Nonetheless, it is unclear how differences in the disinhibition of later feedback pathways would explain early visual processing differences seen in grapheme–colour synaesthetes [19]. Together, these results provide evidence against the disinhibited feedback model of synaesthesia.

8. The cross-activation theory

The cross-activation theory was proposed to explain grapheme–colour synaesthesia and was inspired by its congenital nature and the adjacency of the VWFA (the grapheme processing area) and V4 (a colour processing area) [45,60]. This theory suggests that genetic factors lead to decreased pruning of neural connections, resulting in the *abnormal* connection of two sensory regions. Thus, while V4 and the VWFA are initially connected in all individuals (suggesting that all individuals are born synaesthetes; [61,62]), this connection is pruned away in non-synaesthetes during development. These abnormal connections then lead to a 'cross-activation' of concurrent experiences in the presence of an inducer (i.e. graphemes evoking colours). The cross-activation model, when extended to other forms of synaesthesia, suggests hyper-connectivity between brain regions specific to the form of synaesthesia. For example, grapheme–colour synaesthetes have a hyperconnected V4 and VFWA, and tone–colour synaesthetes a hyperconnected V4 and auditory cortex [31,32].

The cross-activation model makes three main predictions: (1) inducer and concurrent modalities should be in densely interconnected regions, (2) genetic factors alter neural pruning and should predict presence of synaesthesia, and (3) synaesthetes should show anatomical pathways that are not present in adult non-synaesthetes.

Evidence for the cross-activation model is mixed. For example, this model first predicts that the synaesthetic experience is largely accounted for by anatomical changes only in the network connecting the inducer and concurrent modalities. DTI-based evidence in grapheme–colour synaesthetes supports this hypothesis to an extent [29,31]. However, critical review of neuroimaging differences in synaesthesia reveals that anatomical and functional alterations in synaesthetes are not regionally specific as hypothesized by this model, but instead are broadly distributed throughout the brain (also see §4) [8,38].

Second, this model predicts that genetic factors lead to decreased pruning between concurrent and inducer modalities in synaesthetes. Thus, synaesthesia should have a strong genetic component and the genetic factors implicated in synaesthesia should play a critical role in neural pruning. Developmental synaesthesia has indeed been documented to be largely heritable and studies show that there is 73.9% concordance of synaesthesia in monozygotic twins [63]. Tilot *et al.* [64] provided preliminary evidence that genetic factors common to three synaesthetic families may play a role in axonogenesis, in support of the view that genetic differences affect connectivity differences in synaesthetes. However, genetic differences and altered axonogenesis only explain the predisposition of an individual to acquire synaesthesia and not the exact form of synaesthesia that will be acquired. Furthermore, since most of the neural pruning occurs early on in development, differences between synaesthetes and non-synaesthetes should be seen early in life. Indeed, synaesthetic associations are observed at least by age 6; however, they do not become consistent until later adolescence [65]. The cross-activation theory does not directly explain the inconsistency of associations throughout childhood or how novel associations can be acquired through training [56,65] or following foreign language exposure [66] during adulthood.

The cross-activation model also emphasizes that the connections in synaesthetes are unique, critical and sufficient for synaesthetic experiences to arise since they are hypothesized to be pruned away during typical development of non-synaesthetes. However, research over the past 10 years has shown that connections linking sensory regions are present not only during development, but also through adulthood in all individuals (for reviews, see [67,68]). For example, the cross-activation model suggests that auditory and visual areas should be anatomically connected by pathways that are unique to tone–colour synaesthetes, and that the presence of these connections is what gives rise to these synaesthetic experiences [27,69,70]. However, substantial research from human and non-human primates indicates that monosynaptic axons directly link auditory and visual areas in all individuals [71,72]. Moreover, these connections serve vital roles in everyday sensory communication. For example, simple sounds can elicit changes in visual cortex even when no visual stimuli are present [73–79]. Indeed, auditory activity modulates the excitability of the visual cortex [73,80–82], which leads to an improved detection and discrimination of visual stimuli [74,75,83,84]. These results underscore that differences between synaesthetes and non-synaesthetes are not completely explained by the existence of anatomical pathways between inducer and concurrent modalities.

Critically, one could argue that the cross-activation theory could be modified to allow for the existence of the pathways mentioned above in all individuals by suggesting that these pathways are simply stronger in synaesthetes. However, as described above, the literature identifying these structural differences is mixed. No longitudinal study has systematically shown that synaesthesia is a consequence of selective sparing of these connections. Furthermore, the cross-activation theory predicts that synaesthesia cannot be induced or acquired unless there is enough time and reason that causes reorganization of anatomical networks in non-synaesthetes. However, research shows that synaesthesia can be acquired quickly as a result of sensory deprivation or alterations in cortical excitability [55]. Recent evidence

from our laboratory indicates that auditory–visual synaesthesia can be induced in 50% of undergraduate non-synaesthetes with as little as 5 min of visual deprivation [85]. Indeed, patients with neural trauma leading to sensory deprivation who acquire synaesthesia tend to do so within 1–3 days (though onset can occur after several months or not at all) [86,87]. Drugs like lysergic acid diethylamide (LSD), mescaline and psilocybin among others can also induce transient synaesthetic experiences in minutes that last for only a few hours [16]. The cross-activation model fails to explain how synaesthesia can be acquired in a short span of time.

Why do acquired synaesthesias (due to drugs or sensory deprivation) fail to fit into the cross-activation framework? One justification often given is that acquired synaesthesias are completely different from developmental synaesthesia in their neural origin and phenomenological properties. The strongest argument to this effect is the lack of consistency in associations during induced synaesthesia. However, several researchers have discussed [12,13] that consistency is not a required trait of synaesthetic associations, especially during onset [65]. The cross-activation framework thus requires acquired and induced synaesthesias to be due to separate neurobiological mechanisms, with very limited research suggesting existence of such a discrepancy. Alternatively, it remains possible that a single model can account for developmental, acquired and induced synaesthesias.

9. Need for a new model

According to the disinhibited feedback model of synaesthesia, the cross-sensory experiences in synaesthesia arise due to the disinhibition of feedback from higher-level brain areas to the concurrent modality. The major evidence against this long-range disinhibited feedback model is that the delay between activity in the inducer and concurrent is too quick, such that there is no activation in higher processing areas before onset of activity in concurrent. On the other hand, the cross-activation model suggests that synaesthetes have decreased pruning and strengthened connections between inducer and concurrent. The major limitations of this model are that it assumes acquired synaesthesias are inherently different from the developmental form, and that the connectivity differences between synaesthetes and non-synaesthetes are often seen in areas other than those expected according to the model. Along with the problems discussed above with each model, the previous models of synaesthesia (a) fail to predict the broader phenotype of synaesthesia, (b) do not predict the formation of new associations in synaesthesia, and (c) cannot explain cortical excitability differences in synaesthetes nor (d) how synaesthesia can be induced by modulating the cortical excitability of primary sensory areas.

More generally, the cross-activation model emphasizes a genetic basis for the differences between synaesthetes and non-synaesthetes. However, it cannot account for why individuals with a similar genetic composition sometimes have different forms of synaesthesia [63] and why there are individual differences in onset age for synaesthesia [65]. Furthermore, if the connections between regions are pruned during development, synaesthetic associations cannot be acquired without substantial reorganization. However, individuals with synaesthesia can quickly develop (in as little as 10 min) new inducer–concurrent associations in adulthood [66,88]. Furthermore, research indicates that mood, even within the normal range, affects synaesthetic colours experienced by grapheme–colour synaesthetes [89]. Modulations of the synaesthetic experiences such as changes in the concurrent colour in grapheme–colour synaesthesia or reduction of the number of inducers over time have been self-reported by synaesthetes [2,90–92]. The cross-activation theory and the disinhibited feedback model cannot explain why only some stimuli in the inducer modality produce a concurrent sensation but others do not. They fail to explain how new associations develop or are altered during adulthood. These models do not predict the developmental trajectory of associations—that they are inconsistent when first acquired (during development or adulthood) and become consistent over time [65,66,93].

Lastly, these models cannot account for induced synaesthesia in healthy adults by increased cortical excitability. For example, increasing sensorimotor excitability of non-synaesthetes using transcranial direct current stimulation (tDCS) results in behavioural patterns that mimic the characteristics of mirror-touch synaesthesia [55]. Indeed, both the cross-activation model and disinhibited feedback model cannot explain how synaesthesia can be caused by changes in cortical excitability (if connections are already pruned or if hyperexcitability is induced in earlier processing areas than the multisensory nexus).

10. The stochastic resonance model of synaesthesia

A neural model of synaesthesia should be able to explain how synaesthetic experiences arise (developmentally and through acquisition or induction). Additionally, as synaesthetes demonstrate numerous other trait-like differences, a holistic model of this phenomenon should account for these broader phenotypical differences. Considering the evidence reviewed, we propose a new model of synaesthesia, suggesting that a simple change in levels of neural noise in the sensory systems can lead to the experience of synaesthesia (both acquired and developmental forms), as well as produce a broader phenotype of anatomical, functional and perceptual changes seen in synaesthetes.

While engineers often focus on improving mechanical systems by noise-reduction and filtration, biologists, especially neuroscientists, have discovered the presence and importance of noise in the neural system [94–96]. One such critical role of neural noise, counterintuitively, is to increase the quality of signal transmission or detection [20]. This improvement in signal detection is achieved through the principles of stochastic resonance. Stochastic resonance is a phenomenon popularly studied in physics, in which an increase in the input noise can result in an improvement in the output signal-to-noise ratio [21]. Thus, noise makes a system more excitable through stochastic resonance [97] and stochastic resonance can be broadly defined as 'noise benefits' in the context of neural systems (see [98] for review and figure 1 for a simple graphical representation). In one specific application of stochastic resonance, adding noise can be beneficial to attain synchronization among coupled excitable systems; this is also known as stochastic synchronization [97,99–103].

Here, we propose a neural model of synaesthesia based on the principles of stochastic resonance and synchronization (figure 2). Previous models of synaesthesia suggest altered connectivity between brain regions as an explanation for

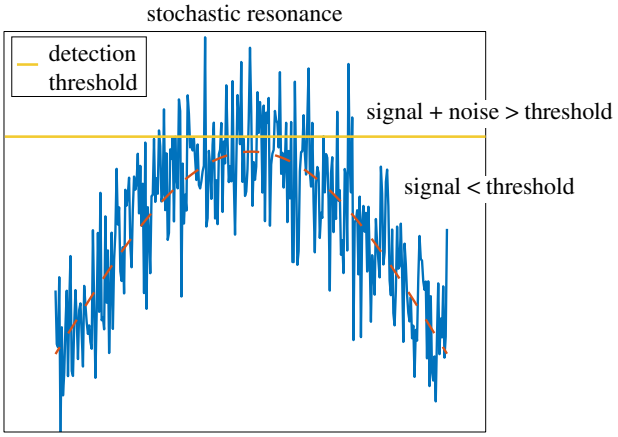

Figure 1. Graphical representation of stochastic resonance. The red dashed line shows a signal in the absence of noise, the blue line this signal in the presence of noise and the horizontal orange line the detection threshold. In isolation, the signal remains below detection threshold, but with the addition of noise it surpasses this threshold. (Online version in colour.)

synaesthetic experiences, while largely ignoring the broader perceptual changes. By contrast, the stochastic resonance model suggests that the phenotype of synaesthesia primarily arises due to higher levels of noise in the concurrent modality (figures 3 and 4). Normal activity sent along pre-existing multisensory connections by the inducer hyperactivates the concurrent modality through stochastic resonance, leading to the additional sensory experience in the concurrent sensory system.

This model argues that the major difference between synaesthetes and non-synaesthetes is noise levels in the concurrent modality and not the neuroanatomical connections between the inducer and the concurrent. Specifically, as anatomical connections linking the sensory systems are present and functionally important in all individuals [71,72] (see §8 for detailed discussion), one sense can modulate activity in a second [74,75,83,84]. However, these cross-sensory signals are typically only modulatory, such that a sound will change the excitability of visual neurons but will not cause visual neurons to generate action potentials [74,81,104], explaining why these cross-sensory modulations do not tend to reach perceptual awareness in non-synaesthetes. However, in the presence of higher sensory noise in synaesthetes (e.g. increased noise in visual areas), these cross-sensory signals could be sufficient to produce supra-threshold activity in the concurrent modality owing to stochastic resonance, leading to the experience of synaesthesia. Thus, this model predicts that the associations one experiences in synaesthesia initially change each time synaesthesia is evoked, based on the current state of the concurrent modality. However, with repeated and consistent evocation of these supra-threshold experiences, the synaesthetic associations would be predicted to stabilize over time. For example, a grapheme–colour synaesthete early in development will have a synaesthetic experience of different colours on every encounter with the number 2 and only after a significant time would the association between 2 and a specific hue become consistent. Indeed, this account is consistent with the wealth of evidence indicating that synaesthetic associations are based on experiences in the environment and are refined over several years [65].

The SRS is based on four main assumptions: (1) synaesthesia occurs through common pathways that are present and functionally important in all individuals, (2) synaesthetic associations are unpredictable at onset and stabilize over time, (3) neural noise is higher in the concurrent modality in synaesthetes than non-synaesthetes, and (4) the broader phenotype of cognitive, perceptual, anatomical and functional differences in synaesthetes occurs in response to the combined presence of increased neural noise and the resulting years of experiencing synaesthesia. Here, we review evidence based on the current literature supporting this model.

11. Evidence supporting the stochastic resonance model

The first assumption of this model is that synaesthesia occurs through pathways that are present and functionally relevant in all individuals. This assumption is consistent with the observation made by several other researchers [105–110] that synaesthesia may be an extension of typical multisensory processes. In addition to physiology research supporting the presence of these connections (also reviewed in §8), additional support comes from the ability of certain drugs like LSD to induce synaesthesia in non-synaesthetic adults in a transient fashion [14]. Human neuroimaging research shows increased resting state activity in the visual cortex following LSD induction compared with placebo control [111,112], indicating that psychedelic drugs may give rise to synaesthetic experiences by increasing the basal neural activity in the visual cortex, which in turn could lead to stochastic resonance between the inducer and the visual cortex.

If cross-sensory anatomical connections are present and functionally relevant in the general population, then why are not all individuals synaesthetes? According to the stochastic resonance model of synaesthesia, modulations of the concurrent modality by the inducer are not strong enough to breach thresholds and reach awareness in normal settings. Functionally, this might be because bottom-up sensory input into the concurrent modality is several times stronger than the modulatory effects of the inducer. Thus, the proclivity to override any signal from the inducer makes detection and stabilization of synaesthesia impossible in non-synaesthetes in most natural contexts. However, non-synaesthetes can detect these modulations when this sensory input is removed, such as under sensory deprivation [113] and in special laboratory settings. Several studies have shown that sounds modulate visual cortex [73,74,81,84] in non-synaesthetes. For example, light flashes that are coupled with two tones are perceived as two flashes instead of one [114]. Similarly, auditory stimulation can lead to the perception of a second phosphene during stimulation of the occipital lobe [115]. Furthermore, sensory deprivation caused by either short-term eye-closure or traumatic injury can lead to even the induction of auditory–visual synaesthesias [86,87]. Therefore, if the synaesthetic experiences are simply a consequence of the modulations reaching perceptual awareness (through stochastic resonance), then amplifying the signal in the concurrent modality should increase the perception of synaesthetic experiences. Animal research shows that drugs like LSD do exactly this by altering noise levels in the visual cortex [116]. Drug-induced synaesthetic experiences thus might be a consequence of inducer modulations reaching awareness owing to altered noise in the concurrent modality.

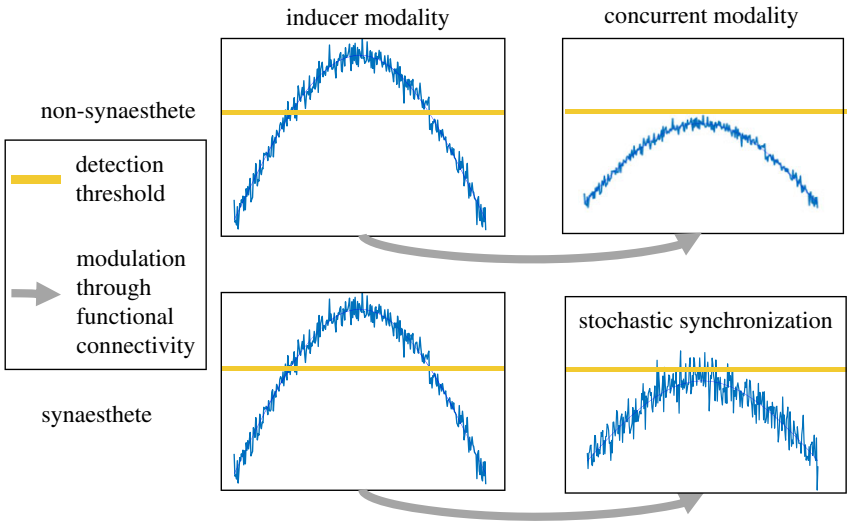

Figure 2. Graphical representation of how stochastic resonance leads to synaesthesia. The blue line shows a signal in the presence of noise, the horizontal orange line the detection threshold, and the grey arrow modulatory functional connections present in synaesthetes and non-synaesthetes alike. Increased noise in the concurrent modality of synaesthetes leads to stochastic synchronization between the inducer and the concurrent. Thus, the sub-threshold modulatory effects breach detection thresholds, leading to synaesthetic experiences. (Online version in colour.)

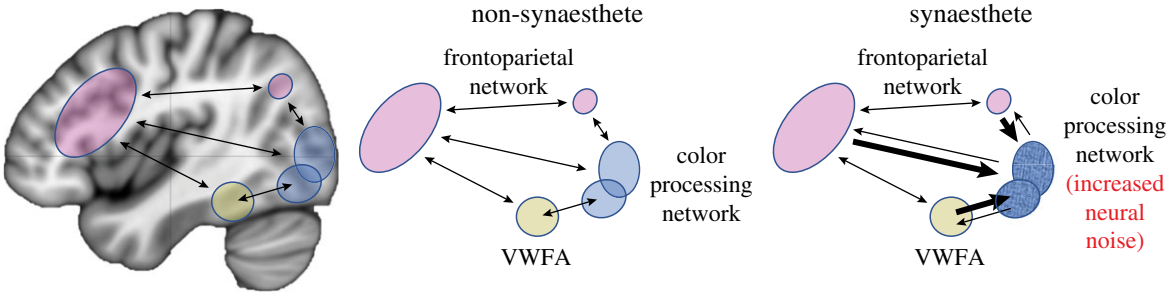

Figure 3. A comparison between non-synaesthetes and grapheme–colour synaesthetes based on the stochastic resonance model. Synaesthetes have higher levels of noise in the colour processing network, which leads to stochastic synchronization between the VWFA and colour processing network. The colour processing areas also have greater cortical excitability and increased connectivity with other frontoparietal areas in non-synaesthetes. (Online version in colour.)

The strength of the SRS is that it can explain developmental and acquired/induced synaesthesias in the same framework. The main argument against acquired synaesthesia being genuine is its inconsistent nature [15]. The SRS rather highlights this aspect and emphasizes that synaesthetic associations are not fixed at onset and stabilize over the course of development in all forms of synaesthesia. These assumptions are supported by Simner & Bain [65], showing that children aged 6–7 are limited to 34% consistent associations on average (e.g. around 12 letters and numbers) and the longitudinal tracking demonstrates that the number of consistent associations increases with age to 48% by age 7–8 and 71% by age 10–11. Interestingly, some children lose their synaesthetic experiences during this period, further highlighting the idiosyncratic nature of synaesthetic associations during development. The associations not only are inconsistent during childhood but also are inconsistent in adult synaesthetes during the formation of new associations. For example, when adults learn a new language, synaesthetic associations that emerge may initially be inconsistent within the first session, but typically become consistent over time [66].

The SRS does not explicitly predict which associations a synaesthete acquires or how they stabilize over time. However, we hypothesize that repeated exposure and usefulness of the associations will be key factors in consolidating these associations. Specifically, repeated supra-threshold activation of the concurrent modality through stochastic resonance may increase the strength of connections between inducer and concurrent through Hebbian learning. Partial support comes from research demonstrating that synaesthesia can be trained [56]. During training, the repeated exposure not only allowed the associations to stabilize, but also resulted in individuals experiencing synaesthetic qualia. Similarly, studies suggest that many associations in synaesthesia are based on learned statistical regularities in the environment [117]. This is supported by studies showing that at a population level, non-synaesthetes have similar associations to synaesthetes [118]. That is, individuals implicitly identify and use statistical regularities in the environment. Finally, research additionally indicates that synaesthetic associations may be useful during learning for synaesthetes [119,120], adding ecological validity to why the associations stabilize.

The final and most important assumption of the SRS is the presence of increased neural noise in the concurrent modality of synaesthetes. This requirement for the model is indirectly supported by research showing that (a) synaesthetes have altered processing and excitability in the concurrent modality, (b) the concurrent shows altered neural connectivity, (c) the

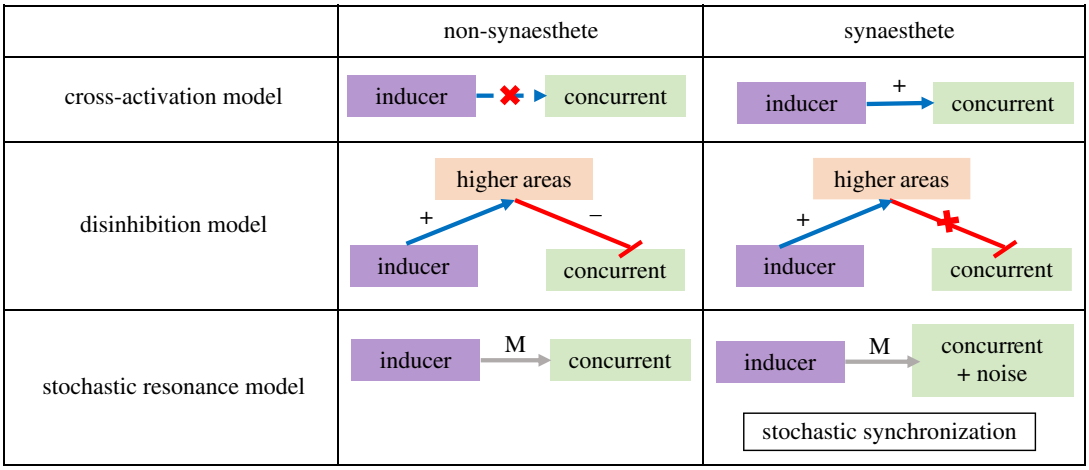

Figure 4. A comparison between non-synaesthetes and synaesthetes according to the cross-activation model, disinhibited feedback model and the stochastic resonance model. 'M' indicates modulatory effects, symbol '+' indicates excitatory input, and symbol '—' represents inhibitory input. According to the cross-activation model, synaesthetes have additional connections between the inducer and concurrent, while the disinhibited feedback model suggests the absence of inhibitory signal from higher areas to the concurrent in synaesthetes. The stochastic resonance model suggests that synaesthetes have higher levels of noise in the concurrent, which leads to stochastic synchronization between the inducer and the concurrent. (Online version in colour.)

inducing modality appears anatomically and functionally normal, and (d) altering noise levels in sensory modalities can induce synaesthesia. In terms of giving rise to synaesthetic associations, increased noise levels in the concurrent modality of synaesthetes should lead to altered processing specifically within the concurrent even in the absence of the inducer. As discussed in §5, grapheme–colour synaesthetes have enhanced visual imagery and normal non-visual imagery [54]. Similarly, grapheme–colour synaesthetes have enhanced colour processing but normal tactile sensitivity, while mirror-touch synaesthetes have higher tactile sensitivity but normal colour perception [48]. Furthermore, research shows that grapheme–colour synaesthetes have early perceptual differences compared with non-synaesthetes in visual processing [19,57,58].

Older animal research in primates and achromatopsia patients suggested that area V4 is the primary colour processing region in the cortex [121–130]. However, a growing body of the literature in animals and humans suggests that colour processing is a broadly distributed process, not restricted to V4, and that colour-selective neurons are present in as early as primary visual cortex [131–142]. Similarly, V4 is involved in more than just colour processing, including the processing of three-dimensional shapes, target comparison, object orientation and motion [143–147]. Thus, we hypothesize that differences between grapheme–colour synaesthetes and non-synaesthetes are present in the broad network of visual areas that process colour information. This hypothesis is supported by research showing that grapheme–colour synaesthetes have greater cortical excitability compared with non-synaesthetes in three different sites in the visual cortex, but do not differ in their motor cortex excitability [52]. Additionally, perceptual differences between grapheme–colour synaesthetes and non-synaesthetes are present in early visual processing [19]. Furthermore, neuroimaging studies suggest that activation differences in synaesthetes and non-synaesthetes are not limited to V4 but are also seen in adjacent regions [8,148]. However, perceptual differences in synaesthetes are not a general feature of the synaesthetic brain but are specific to the concurrent modality (for example, visual, but not auditory, differences in the case of grapheme–colour synaesthesia). The SRS explains the broader phenotype of perceptual differences in synaesthetes through higher noise levels in the concurrent modality. Specifically, perceptual sensitivity is strongly associated with cortical excitability as measured using transcranial magnetic stimulation (TMS)/tDCS [149–151], which indicates a link between cortical excitability and perceptual sensitivity as seen in synaesthetes.

Recent research shows that individuals with autism spectrum disorder (ASD) and synaesthesia share an atypical profile of increased sensory sensitivity [152,153]. Thus, the sensory processing deficits seen in individuals with ASD or Asperger syndrome may explain the observation of a higher incidence of synaesthesia in this population [154–157]. Autism has been associated with an imbalance in excitatory/inhibitory levels in the sensory systems and the social–emotional system [158–162], including altered levels and action of inhibitory gamma-aminobutyric acid (GABA) (see [163] for review). Similarly, autism research also shows that neural variability/neural noise is higher in adults with ASD than in healthy adults [158,162,164]. One could speculate that in the SRS framework, both conditions are due, in part, to the increased neural noise, but differ in terms of where these differences are observed: in autism, there may be a more broadly distributed increase in noise levels, including emotional, limbic and occasionally sensory areas (that in turn cause synaesthesia to arise in such cases), while they are focal and only in sensory regions in synaesthesia. Since the balance of excitatory/inhibitory neurotransmitters controls noise levels in the brain [165,166], a greater understanding of how this balance is altered in both autism and synaesthesia may help clarify the observed link between the two conditions.

The maintenance of neural noise levels in a neural network is modulated by the balance of excitatory and inhibitory neurotransmitter levels [165,166]. Magnetic resonance spectroscopy-based estimation of major inhibitory neurotransmitter GABA and excitatory neurotransmitter glutamate suggests that there is reduced GABAergic action but conserved glutamatergic action in the visual cortex of individuals with ASD compared with healthy controls. This reduction of GABAergic levels affects perceptual suppression

in the visual cortex in autism [167]. Similarly, the *GABRB3* gene, which codes for an important GABA receptor, has been associated with autism and increased tactile sensitivity [168]. GABA levels have also been associated with increased tactile sensitivity as well as visual discrimination ability in a region-specific manner [169,170]. Furthermore, GABA levels are region-specific even in healthy human adults [171,172]. Thus, altered neurotransmitter levels in the concurrent modality can explain the region-specificity (i.e. changes restricted to the concurrent modality) of increased neural noise in synaesthesia.

Altered noise levels in the concurrent modality may also explain observed patterns of altered connectivity in synaesthetes, particularly between the concurrent and connected brain regions. Higher noise levels may lead to repetitive co-activation of the concurrent in the presence of an inducer, leading to increased connectivity between them. Indeed, in epilepsy, which most often occurs owing to hyperexcitable neurons in the medial temporal lobe, even though the seizure begins in a small cluster of neurons, the increased responsivity of this area dramatically alters patterns of connectivity throughout the brain [173–175]. Additional research will be needed to confirm the extent to which this model explains and predicts elements of the synaesthesia phenotype. In synaesthetes, this might be observed as hyper-connectivity between the inducer and concurrent, which is the premise of the cross-activation model. However, according to this model, while increased pathway strength between two modalities can enhance synaesthetic associations, they are not necessary for the development of synaesthesia. This is supported by longitudinal researching showing that neural connectivity between the auditory cortex and somatosensory cortex increased in a synaesthete who acquired sound–touch synaesthesia following a stroke [176]. Similarly, decreased pruning between inducer and concurrent will preserve the connectivity between the two, allowing easier modulation of the concurrent through the inducer via stochastic resonance. In this regard, the SRS is not completely incompatible with the cross-activation model, as it is possible that synaesthesia could emerge from either cause (increased connectivity or increased neural noise). However, we predict that synaesthetes who develop synaesthesia through increased connectivity and not neural noise will have a different phenotype (e.g. no perceptual or excitability changes). Further research should investigate the neural changes in development of both acquired and developmental synaesthesia to explore these possibilities.

If the synaesthetic experiences are guided mainly by the inducer–concurrent stochastic resonance, then how can semantic information or top-down influences lead to differences in synaesthetic experiences [45,177]? Sensory processing at both cortical and thalamic levels is strongly modulated by top-down influences [178–180] (for example, semantic priming can alter visual perception [181]). Interestingly, colour information has also been shown to invoke semantic networks in the brain [182] and semantic networks have been shown to invoke early colour perception [183,184]. Thus, in the SRS model framework, semantic effects observed in synaesthesia are a byproduct of modulatory effects on sensory perception and are not unique to synaesthesia. However, there might be differences in the strength of these modulations between non-synaesthetes and synaesthetes owing to altered connectivity between the concurrent and frontoparietal regions [31,38].

Along with altered connectivity with the inducer, the noisier concurrent also has altered connectivity with other brain regions. For example, in grapheme–colour synaesthetes, the colour processing regions (including primary visual (V1) and V4) might be hyperconnected to other connected regions. This is consistent with research showing activity in neighbouring brain regions other than V4, including texture areas in grapheme–colour synaesthesia [8,148]. Neural noise levels in the early stages of synaesthesia might determine the strength of these connections as well as where they project. Visual cortex will thus have differences in its connectivity to other brain regions that it is normally connected with. This may explain the frontal and parietal connectivity differences observed in synaesthetes [31,38]. Thus, we suggest that the neural connectivity differences in synaesthetes will be more global than merely being restricted to the inducer–concurrent pair (figure 3).

The SRS suggests that the difference between synaesthetes is in the concurrent modality and, therefore, there is nothing unique about the inducer. This is consistent with population-based clustering studies showing that synaesthetes often have more than one form of synaesthesia with a common concurrent (but not always) [185]. Indeed, monozygotic twins may have distinct forms of synaesthesia with different inducers, but will generally share the same concurrent modality [63]. These results demonstrate that during development there is nothing unique about the inducer modality. In this framework, increased neural noise in the inducer modality is not required for development of synaesthesia but might aid stochastic synchronization between inducer and concurrent.

Most of the evidence presented supporting a model of altered neural noise in synaesthetes is indirect. Future research should explicitly test this prediction directly, especially during the onset of synaesthesia. In the next section, we suggest studies that can be used to examine the model's limits as well as future directions for expanding this framework.

12. Future directions

The stochastic resonance model of synaesthesia makes several predictions that can readily be tested. Here, we mention a few:

1. It predicts differences between synaesthetes and non-synaesthetes in terms of their neural noise. Noise measures, such as EEG entropy, can be used to measure variability in neural activity to compare synaesthetes and non-synaesthetes.
2. It suggests that the type of synaesthesia that develops should be based on (a) experiences during development and (b) the sensory modality with an increased level of noise. For example, if one has excessive noise in perceptual colour areas and extensive exposure to musical training early in life then one should be more likely to develop auditory–visual synaesthesia. Similarly, populations more immersed in the use of tonal languages like Chinese should have a greater prevalence of tone–colour synaesthesia. This seems likely since absolute pitch is more prevalent in tonal languages [186,187] and synaesthesia is more prevalent in individuals with absolute pitch [188].

3. There is no critical period to acquire synaesthesia in the SRS framework. However, as neural noise levels are higher during development [189,190], it should be easier to acquire synaesthesia during development. As neural noise levels decrease and stabilize during adolescence, synaesthesia may be lost for some individuals. Indeed, beneficial noise declines in older adults, consistent with reports that synaesthesia weakens or is lost late in life. Conversely, the induction of synaesthesia in adulthood is expected to require external pressure in the form of drugs that increase neural noise in sensory areas, sensory deprivation or potentially extensive training. Longitudinal tracking of synaesthetes in terms of their synaesthetic experiences and associations along with neural measures of noise can verify each of these predictions.
4. Enhanced plasticity present during development can enable neural noise differences in the concurrent modality to produce broader phenotypical differences in synaesthetes. Thus, synaesthetes who acquire synaesthesia earlier in life (when there is greater plasticity) will exhibit more brain-wide differences (global connectivity changes), while those who acquire synaesthesia later will have more restricted differences (largely in the concurrent modality).
5. One way to measure neural noise in the concurrent is to quantify its excitability. Our model suggests that synaesthetes should have increased excitability in the specific concurrent modality and not necessarily other brain regions. It is possible that the expression of synaesthesia (projector versus associator) or the number of synaesthesias one experiences is associated positively with the degree of excitability in a region-specific manner.
6. In developmental synaesthetes, any area that has high input to the concurrent modality should have increased connectivity with the concurrent (owing to stochastic resonance; figure 3). Thus, in synaesthetes, altered connectivity should be seen not only between concurrent and inducer, but also with other brain regions.
7. Cortical excitability, neural noise and excitation/inhibition balance differences should be measurable in synaesthetes even before the onset of synaesthetic experiences. Thus, we should be able to use cortical excitability or neurotransmitter levels as a predictor for whether children of synaesthetes will themselves develop synaesthesia.
8. Similarly, certain drugs induce specific cortical changes (e.g. LSD alters levels of neural noise and connectivity in visual cortex [111,116]). Thus, one should be able to track drug-induced cortical excitability changes in a modality-specific manner to predict the onset and type of synaesthesia induced.

Although synaesthesia is genetic, it only affects the propensity to develop synaesthesia. For example, sometimes only one of a monozygotic pair of twins develops synaesthesia [63]. According to the SRS, the form of synaesthesia and the associations acquired will be determined by environmental factors. However, further research should help develop the exact genetic and molecular mechanisms that alter neural noise and in turn predispose individuals to synaesthesia. Although the cross-activation model can determine the predisposition of an individual to acquire synaesthesia, it cannot predict when (the onset age) an individual will develop synaesthesia or how new associations will develop; future studies, like those mentioned above, will further refine the SRS to address critical issues such as these. Importantly, as recent studies have failed to replicate the findings of concurrent activation and connectivity differences in synaesthetes [8–10], future research should incorporate recent advances in our understanding of normal colour processing to further promote the development of better models of synaesthesia.

Computational models of synaesthesia may advance our understanding of how associations develop between the inducer and the concurrent with stochastic resonance. For example, a recent computational model proposed by Shriki and colleagues demonstrated that synaesthesia can emerge in a neuronal network through changes in neuronal plasticity and sensitivity [191]. This model places developmental and acquired synaesthesias within the same framework, and accounts for increased cortical excitability in synaesthetes compared with non-synaesthetes as well as a monotonic mapping between inducer and concurrent. The SRS partly overlaps with this computational model, and the latter could be extended to test whether synaesthesia is predicted to emerge owing to greater noise in the concurrent modality (as our model predicts). In their current form, the two models make different predictions that can be addressed in future studies: (a) the computational model suggests that the connectivity (cross-talk in their language) between inducer and concurrent modalities is zero in non-synaesthetes, whereas the SRS model predicts that there is a continuum linking synaesthetes and non-synaesthetes, wherein the inducer and concurrent are connected and exhibit sub-threshold cross-talk in non-synaesthetes; (b) the simple computational model, unlike the SRS, is limited to the inducer and concurrent modalities and does not predict brain-wide differences, early perceptual differences between synaesthetes and non-synaesthetes or explain top-down influences on synaesthetic experiences; (c) the SRS, unlike the computational model, does not implicitly require plasticity differences (in duration or amount) during childhood in developmental synaesthesia.

Most of the evidence presented in this article is based on grapheme–colour synaesthesia and does not distinguish between projectors and associators. It would be imprudent to assume the validity of the SRS for different expressions and forms of synaesthesia without further testing. Indeed, it is possible that more than one mechanism underlies different forms of synaesthesia. Similarly, most previous models of synaesthesia, including the SRS, are limited in their ability to explain only the percept in the concurrent but not its non-veridicality (knowledge or awareness that the concurrent percept is not real). The predictive processing theory of sensorimotor contingencies provides one framework that can account for the presence of a percept and yet the absence of veridicality in synaesthesia [192]. Finally, the SRS can be combined with other models and theories to explain different aspects of synaesthesia, such as how associations become consistent through the role of the environment, the non-veridicality of the synaesthetic percepts, and why individuals differ in their experiences (projector versus associator).

13. Conclusion

The stochastic resonance model of synaesthesia can be thoroughly validated with future studies as suggested in the previous section. The model suggests that the various perceptual differences in synaesthetes are not a simple

consequence of cross-sensory experiences but rather a part of the broader phenotype of synaesthesia. We hypothesize that these perceptual differences might provide a better marker of synaesthesia than the conventional correlates such as consistency (which we argue is not a requirement for synaesthetic experiences). The SRS also does not discriminate between types of synaesthesia—induced versus developmental synaesthesia—in terms of providing a neurological basis. The stochastic resonance model of synaesthesia incorporates several of the recent findings from research on the perceptual systems and neuroanatomical connectivity, and addresses limitations in older models to provide a better theoretical framework to understanding the neurological basis of synaesthesia and neural noise in general.

Data accessibility. This article has no additional data.

Authors' contributions. P.L. and D.B. jointly designed the model, and drafted the manuscript. Both authors gave final approval for publication and agree to be held accountable for the work performed herein.

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